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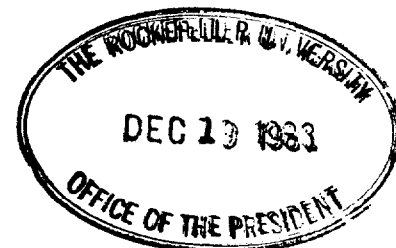
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SANTA BARBARA • SANTA CRUZ

December 9, 1983

DEPARTMENT OF PSYCHIATRY AND  
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UCLA SCHOOL OF MEDICINE  
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Dr. Joshua Lederberg  
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Dear Dr. Lederberg,

Dr. Tarjan asked me to try and respond to your letter concerning the role of kernicterus in mental retardation. This is very hard to do, since there are no recent figures of relevance. The major decrease in kernicterus occurred with the control of Rhesus incompatibility.

The main group of infants at risk now for kernicterus are low birth weight infants. A recent review of infant morbidity (Shapiro, et.al., Pediatrics 72, 408, 1983) found that 6.11% of infants weighed less than 2500 grams at birth and 0.98%, or approximately 1/6, weighed less than 1500 grams; it is this last group that are at greatest risk for kernicterus.

Levine, et.al., (Pediatrics 69, 255, 1982) noted that hyperbilirubinemia is about the commonest medical diagnosis in the newborn, particularly in prematures. 5% of liveborn neonatal autopsies demonstrated kernicterus (Turek, et.al., Pediatrics 69, 267, 1982). If these figures are correct, they translate into 5% of the 46,000 infant deaths per year (using 4,000,000 as the live birth rate per year in the U.S.), or 2,300. Undoubtedly, other factors contributed to some of these deaths (congenital abnormalities, intracranial hemorrhage, etc.).

The best that I can do with regard to "outcomes" for infants weighing ≤1500 grams follows. However, it does not address the issue of kernicterus. Between 1975-79, infant mortality rates decreased for those weighing 1000-1500 grams, and 18% were left with major neuropsychiatric disabilities (Knoblock, et.al., Pediatrics 69, 285, 1982). Shapiro's study quoted above found that about 6% of infants weighing ≤1500 grams at birth had gross motor performance delay (DQ ≤70) and a further 17% were borderline (DQ 70-79) when assessed at 1 year of age.

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The predictive value of serum bilirubin levels, free or total, was poor. Ritter, et.al. (Pediatrics 69, 260, 1982) studied 91 infants weighing <1500 grams at birth; 58% died and of these, 23% showed pathologic evidence of kernicterus. There was no significant difference in either the free or total bilirubin in infants with and without kernicterus. Further, hyperbilirubinemia may result from hemorrhage into a closed space and recent ultrasound studies indicate that nearly 50% of infants weighing <1500 grams have intracranial hemorrhage; this rather than the hyperbilirubinemia may be the cause of brain damage.

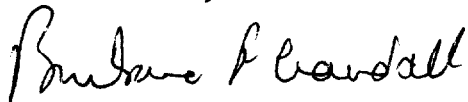
I think I can summarize this data in the following way:

1. Hyperbilirubinemia is common in premature infants, particularly in those weighing <1500 grams (the incidence in different reports varies between 2-16%).
2. Serum bilirubin levels appear to be a poor predictor of kernicterus.
3. Hyperbilirubinemia may result from a number of factors, including brain hemorrhage.
4. Brain hemorrhage itself may be the cause of subsequent neurologic impairment, including mental retardation.
5. In addition, primary hyperbilirubinemia almost certainly contributes to neurologic impairment and mental retardation. This probably results from changes in the blood-brain barrier (Levine, et.al., Pediatrics 69, 255, 1982) allowing bilirubin into the brain.

Your proposed studies would be relevant to this last group. It would be very difficult to separate the last two groups, or to predict the number of cases of mental retardation prevented.

I hope this information will be of help to you. Please let me know if I can help you further.

With best wishes,



Barbara F. Crandall, M.D.  
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Director, Prenatal Diagnostic Center

BFC:as

cc: George Tarjan, M.D.